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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,069	12/04/2003	Carsten Muenk	532792000100	9175
35938	7590	09/12/2006		
BIOTECHNOLOGY LAW GROUP C/O PORTFOLIOIP PO BOX 52050 MINNEAPOLIS, MN 55402				
			EXAMINER	
			HUMPHREY, LOUISE WANG ZHIYING	
			ART UNIT	PAPER NUMBER
			1648	

DATE MAILED: 09/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/729,069

Applicant(s)

MUENK ET AL.

Examiner

Louise Humphrey, Ph.D.

Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 26 June 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-14 and 21-32 is/are pending in the application.
- 4a) Of the above claim(s) 3,7 and 8 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-6,9-14 and 21-32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 6/26/06.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_.

### DETAILED ACTION

This Final Office Action is in response to the After-Final amendment filed on 26 June 2006. Claims 22-32 are newly added. Claims 1-14 and 21-32 are pending, of which claims 3, 7, and 8 are withdrawn from consideration and claims 1, 2, 4-6, 9-14 and 21-32 are under examination.

It is noted that the Examiner omitted the sentence "Claims 1, 2, 4-6, 9-14, and 21 are rejected under 35 U.S.C. §103(a) as being unpatentable over Moir *et al.* (1996) in view of Mohler *et al.* (1996)" on top of page 5 of the Office Action mailed on 27 March 2006. Examiner apologizes for her oversight.

### ***Information Disclosure Statement***

The information disclosure statement (IDS) filed 26 June 2006 is being considered by the examiner.

### ***Claim Rejections - 35 USC § 103***

The rejection of claims 1, 2, 4, 5, and 9-14 under 35 U.S.C. §103(a) as being obvious over Bieniasz *et al.* (1997) in view of Mohler *et al.* (1996) is **maintained and extended** to new claims 22, 23, and 25-32. Applicants' arguments filed on 26 June 2006 have been fully considered but they are not persuasive. Applicants argue that there was no motivation to combine the cited documents.

Applicants allege that Mohler fails to mention cell fusion assays mediated by a viral envelope protein and therefore there is no motivation to combine it with Bieniasz.

Art Unit: 1648

Applicants argue that the specific applications suggested in the "Conclusions" section of Mohler do not include the claimed method: assessing cell fusion mediated by a viral envelope protein. Examiner respectfully disagrees. Although Mohler does not state exactly the same words, a cell fusion mediated by a viral envelope protein involving the interaction of the viral envelope protein with the host cell membrane receptor CD4, which is a glycoprotein, falls under the category of proteins derived from two active genes being co-incident or co-localizing in a cell and protein-protein interactions. Therefore, contrary to Applicants' allegations, Mohler addresses the same problem to be solved as Bieniasz.

In response to Applicants' allegation that the documents themselves provide no motivation for modification, there is no requirement that an "express, written motivation to combine must appear in prior art references before a finding of obviousness." See *Ruiz v. A.B. Chance Co.*, 357 F.3d 1270, 1276, 69 USPQ2d 1686, 1690 (Fed. Cir. 2004). For example, motivation to combine prior art references may exist in the nature of the problem to be solved (*Ruiz* at 1276, 69 USPQ2d at 1690) or the knowledge of one of ordinary skill in the art (*National Steel Car v. Canadian Pacific Railway Ltd.*, 357 F.3d 1319, 1338, 69 USPQ2d 1641, 1656 (Fed. Cir. 2004)).

Mohler clearly suggests a modification that can be applied to the cell fusion system taught by Bieniasz so that the detection of cell fusion will be easier and more accurate. The replacement of the reporter gene of Bieniasz with the complementing  $\beta$ -galactosidase ( $\beta$ -Gal) reporter gene of Mohler results in the advantage of specific detection of the interaction between CD4 and HIV envelope glycoprotein and reduction

Art Unit: 1648

of background signals and false signals, which is well in the knowledge generally available to one of one skilled in the art and suggests the desirability of the claimed methods. "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art." *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). See MPEP §2143.01 [R-3]. In the instant case, the combined teachings of Mohler and Bieniasz, knowledge of one skilled in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art the modification of the SEAP reporter system of Bieniasz to the complementing  $\beta$ -galactosidase reporter gene of Mohler.

Since Applicants combined the rebuttal to both 103 rejections in their response filed on 26 June 2006, the rejection of claims 1, 2, 4, 5, and 9-14 under 35 U.S.C. §103(a) as being obvious over Moir *et al.* in view of Mohler *et al.* (1996) is **maintained and extended** to new claims 22, 23, and 25-32 for the same reasons as above.

#### New Rejection

Claims 1, 2, 4-6, 9-14, and 21-32 are rejected under 35 U.S.C. §103(a) as being obvious over Moir *et al.* (1996) in view of Moosmann *et al.* (1996, as filed in IDS on 26 June 2006).

The instant invention is further limited to the specific embodiments of the N-terminal alpha region of  $\beta$ -Gal with various size limitations.

Moir *et al.* disclose a first cell co-expressing CD4- $\beta$ -Gal and a second cell expressing HIV-1 envelope protein and Rev (page 812, Materials and Methods). Moir *et al.* suggests applying this fusion assay system to the search for potential fusion blocking agents (last sentence). Moir *et al.* do not disclose the complementation of the alpha and omega fragments of  $\beta$ -Gal.

Moosmann *et al.* describe the alpha complementation of  $\beta$ -Gal in mammalian cells, specifically, HeLa cells, and disclose that the optimum length of the alpha complementing peptide is about 85 amino acids. Moosmann *et al.* further disclose one alpha peptide spanning from amino acid 1 to amino acid 85 and an omega complementing peptide lacking a region spanning amino acid 9 to amino acid 37 (Figure 1). Moosmann *et al.* explicitly suggest this approach for easy monitoring of various fusion proteins in eukaryotic systems (last paragraph).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the  $\beta$ -Gal of Moir *et al.* such that the reporter gene is split into two fragments expressed by two separate cells to be tested in a fusion assay rather than expressing the full length  $\beta$ -Gal in a single cell. One having ordinary skill in the art would have been motivated to do this so that the complementation of the reporter gene does not occur between adjacent single transduced cells, indicating that cell fusion is a prerequisite for the formation of complemented enzyme. In other words, this modification of the cell fusion assay reduces false positive signals and increases the accuracy of the method. There would have been a reasonable expectation of success, given that the alpha complementation has been widely exploited for studies in

Art Unit: 1648

prokaryotes and that co-expression of alpha and omega peptides resuscitates enzymatic  $\beta$ -Gal activity that is absent in the single components, as taught by Moosmann *et al.* Thus, the invention as a whole was clearly *prima facie* obvious,

Art Unit: 1648

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

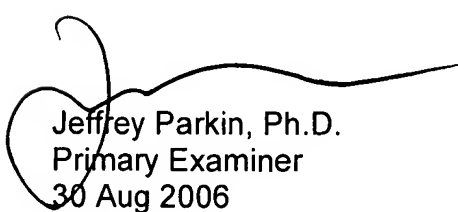
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### ***Contact Information***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Jeffrey Parkin, Ph.D.  
Primary Examiner  
30 Aug 2006

*lvh*  
8/30/06